

REMARKS

Please review and enter the following remarks summarizing the interview conducted on November 16, 2004, wherein an Interview Summary, Form PTOL-413, was provided by the Examiner to counsel for Applicants.

During the interview, the rejections in the Office Action mailed September 13, 2004, were discussed.

1. Brief description of exhibits or demonstration: None.
2. Identification of claims discussed: 1 and 18-23.
3. Identification of art discussed: None.
4. Identification of principal proposed amendments: It was agreed that the following amendments should resolve the outstanding §112 issues.

21. (currently amended): A serotonin 5-HT₃ receptor antagonistic agent or partial activator for therapeutic treatment of condition of irritable bowel syndrome or digestive tract functional disorder, or condition of diarrhea, comprising as an active ingredient, an effective amount of a substance selected from the group consisting of ~~the compound according to claim 1~~ 5-chloro-2-(1-homopiperaziny)-7-methylbenzoxazole, a pharmaceutically acceptable salt thereof, a hydrate thereof, and a solvate thereof.

22 and 23. (canceled).

5. Brief Identification of principal arguments: The claimed compound is unexpectedly superior over the prior art. As evidence, counsel for Applicants directed the Examiner's attention to Test Examples 2 and 4 and the data in the tables at pages 38 and 40 of the specification.

6. Indication of other pertinent matters discussed: The status of the outstanding double patenting rejections.

7. Results of Interview: The Examiner stated that she would like Applicants to provide information that places the results from Test Example 2 in a context that would allow her

to better gauge the significance of the values reported in the table at page 38 of the specification. With respect to Test Example 4 and the data in the table at page 40 of the specification, the Examiner misunderstood the entry for "Compound of Example 1(b)." Counsel pointed out that the notation "N.D." means that the concentration of the test compound was not changed before and after the incubation, as indicated just below the table at page 40. With respect to the double patenting rejections, the Examiner agreed that if Applicants are able to persuade her of the significance of the data in the tables at page 38 and 40 of the specification, the double patenting rejections should all be withdrawn.

It is respectfully submitted that the above STATEMENT OF SUBSTANCE OF INTERVIEW complies with the requirements of 37 C.F.R. §§1.2 and 1.133 and MPEP §713.04.

Upon entry of the claim amendments, Claims 1 and 18-21 will be all the claims pending in the application.

Consistent with the discussion held during the interview, Applicants have amended Claim 21 and canceled Claims 22 and 23. Amended Claim 21 is an independent claim combining the subject matter of Claims 21 and 22.

No new matter has been added.

Referring to Section Nos. 1 and 2, at pages 2 and 3 of the Office Action, the Examiner has maintained the §103 obviousness rejections of Claims 1 and 18-24. That is, Claims 1 and 18-24 stand rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Sato, *et al* (Journal of Medicinal Chemistry), and Claims 1 and 18-24 stand rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over EP 0 806 419 ("EP '419").

Applicants respectfully traverse.

The presently claimed compound's unexpectedly superior suppressing action against diarrhea and the compound's unexpectedly superior metabolic stability rebuts any *prima facie* case of obviousness. In order to prove that the claimed compound is unexpectedly superior over the prior art, Applicants direct the Examiner's attention to Test Examples 2 and 4, at pages 37-38 and 39-40, respectively, and in particular, to the tables at pages 38 and 40 of the specification.

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Test Example 2 and the table at page 38 shows that the ED₅₀ value (mg/kg) for the hydrochloride of E test compound (which is the same compound as Sato's compound 6v and the same compound as disclosed at page 5, line 19, of EP '419) is more than 16 times greater than the ED₅₀ value (mg/kg) for the compound of Example 1(b) (which is a salt of the compound of Claim 1 with hydrochloric acid).

Test Example 4 and the table at page 40 shows that the compound of Example 1(b) was completely stable in terms of metabolic stability (no change in its concentration before and after incubation in Test Example 4), whereas the hydrochloride of E test compound suffered significant metabolic degradation (a metabolic rate of 0.50 nmol/min/mg in Test Example 4).

Furthermore, consistent with the discussion held during the interview, Applicants are submitting herewith the Rule 132 Declaration of Dr. Yasuo Sato, a co-inventor of the present application. Dr. Sato's Declaration provides the Examiner with the information she requested for placing the results from the test examples in a context that allows her to better gauge the significance of the values reported in the tables.

In light of Dr. Sato's Declaration, Applicants respectfully request the withdrawal of the §103 rejections.

Referring to the §112 rejections presented at Section No. 3 (pages 3 and 4) of the Office Action, Applicants have amended Claim 21 and canceled Claims 22 and 23, as discussed during the interview. Accordingly, Applicants request the withdrawal of the §112 rejections.

Referring to Section Nos. 4 and 5 at pages 4 and 5 of the Office Action, the Examiner has maintained the obviousness-type double patenting rejections based on U.S. Patent No. 6,037,342 and U.S. Patent Application No. 10/219,496.

Applicants respectfully traverse.

The double patenting rejections are traversed for the same reasons as the §103 rejections based on Sato and EP '419. Any analysis employed in an obviousness-type double patenting rejection must parallel the guidelines for analysis of a §103 obviousness determination, including the evaluation of all objective evidence of nonobviousness. Therefore, in light of Dr. Sato's

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Declaration, Applicants respectfully request the withdrawal of the obviousness-type double patenting rejections.

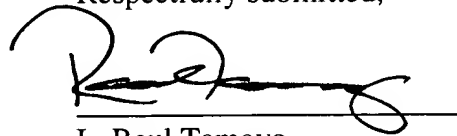
Finally, at Section No. 7, pages 5 and 6 of the Action, Claim 18 has been rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over Claims 1-3 of U.S. Patent No. 6,552,057.

The '057 Patent issued from a divisional application in a line of divisional applications having as the parent application the application that issued as the '342 Patent. Therefore, as with the double patenting rejections based on the '342 Patent and the '496 Application, Claim 18 is not an obviousness-type double patenting of Claims 1-3 of the '057 Patent for the same reasons that Sato and EP '419 fail to render obvious Claims 1 and 18-24. In light of Dr. Sato's Declaration, Applicants respectfully request the withdrawal of this obviousness-type double patenting rejection.

Reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,



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